

Amendments to the Specification:

Please replace the paragraph beginning at line 23, page 7 with the following amended paragraph:
Figure 4C 1C1-1C8 Cell surface CD69 expression in representative positive cell clones.

Please replace the paragraph beginning at line 3, page 8 with the following amended paragraph:
Figure 2C 2C1-2C2 Northern blot analysis of SLIM expression

Please replace the paragraph beginning at line 14, page 8 with the following amended paragraph:
Figure 3A 3A1-3A4 Inhibition of CD69 upregulation by SLIM and SLAP in tTA-BJAB cells

Please replace the paragraph beginning at line 21, page 8 with the following amended paragraph:
Figure 3B 3B1-3B3 Anti-CD3 induced CD69 expression is inhibited by SLIM

Please replace the paragraph beginning at line 35, page 8 with the following amended paragraph:
Figure [4] 4A1-4A4 The N-terminal myristylation site and C-terminal unique regions of SLIM are required for inhibition of antigen receptor signaling

Please replace the paragraph beginning at line 18, page 9 with the following amended paragraph:
Figure 6 6A1-6A5, 6B1-6B5, 6C1-6C3, 6d1-6D2 SLAP-2 (SLIM) inhibits antigen receptor signaling in Band T lymphocytes

Please replace the paragraph beginning at line 37, page 9 with the following amended paragraph:
Figure 7 7A1-7A2 SLAP-2 represses antigen-induced calcium mobilization in BJAB and Jurkat cells.

Please replace the paragraph beginning at line 7, page 10 with the following amended paragraph:
Figure 8 8A1-8A3, 8B1-8B3 The N-terminal myristoylation site and C-terminal unique regions of SLAP-2 are required for inhibition of antigen receptor signaling.

Please replace the paragraph beginning at line 15, page 9 with the following amended paragraph:
Wild type SLIM, SLIM-myr or SLIM-ΔC were immunoprecipitated as in A and immunoblotted with anti-Cbl antibodies. WT SLIM and SLIM-myr but not ~~SLIM-ΔC~~ SLIM-ΔC associate with Cbl after antigen stimulation.

Please replace the paragraph beginning at line 2, page 63 with the following amended paragraph:

SLIM associates with tyrosine phosphorylated proteins following antigen receptor engagement. Signaling through the TCR or BCR results in a rapid increase in tyrosine phosphorylation of numerous intracellular proteins, initiated by Src family and Syk/ZAP70 kinase activation. These early signaling events ultimately result in transcriptional activation, upregulation of surface antigens, and other lymphocyte effector functions. Adapter proteins play an important intermediary role in integrating upstream signals to produce biological function. In order to investigate the nature of SLIM signaling complexes, epitope-tagged versions of SLIM, SLIM-myr, or ~~SLIM-DC~~ SLIM-ΔC were stably introduced into BJAB cells. All three proteins became associated with a number of tyrosine phosphorylated proteins following BCR stimulation (Fig. 5A), demonstrating that SLIM indeed participates in BCR signaling pathways. Interestingly, a prominent phosphoprotein of approximately 110 kD was absent in the immunoprecipitates of ~~SLIM-DC~~ SLIM-ΔC (Fig. 5A), which we subsequently identified as the RING finger ubiquitin ligase Cbl (Fig. 5B). Cbl has been previously shown to be a negative regulator in TCR signaling pathway and to constitutively interact with the C-terminal region of SLAP as demonstrated in both a yeast two hybrid system and mammalian cells. However, the association between SLIM and Cbl in B cells was inducible following antigen receptor stimulation, suggesting SLIM and SLAP may utilize different mechanisms to recruit other signaling partners. It would be possible for SLIM to function as an inhibitory adapter by either recruiting a negative regulator into the signaling pathway and/or by directly blocking the function of a positive regulator. Our results suggest that SLIM functions via the former mechanism in antigen receptor signaling cascades.

Please replace the paragraph beginning at line 22, page 63 with the following amended paragraph:

SLIM associates with tyrosine phosphorylated proteins in B cells. Sorted tTA-BJAB cells infected with epitope-tagged wild type SLIM, SLIM-myr or ~~SLIM-DC~~ SLIM-ΔC were stimulated with anti-IgM F(ab')₂ for 2 mins, lysed and SLIM was immunoprecipitated using anti-FLAG antibodies. Immunoprecipitated proteins were subjected to SDS-PAGE and immunoblotted with anti-phosphotyrosine antibodies. SLIM associates with tyrosine phosphorylated proteins of approximately 110 and 70 kDa after antigen stimulation. The ΔC

mutant lacks the 110 kDa SLIM-associated phosphoprotein. Lower panel: Reprobe with anti-FLAG. (Figure 5).

Please replace the paragraph beginning at line 30, page 63 with the following amended paragraph:

SLIM interacts with Cbl in B cells. Wild type SLIM, SLIM-myr or ~~SLIM-DC~~ SLIM-ΔC were immunoprecipitated as in A and immunoblotted with anti-Cbl antibodies. WT SLIM and SLIM-myr but not SLIM-DC associate with Cbl after antigen stimulation. (Figure 5)